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**Overview****Useful For**

Distinguishing large deletional hereditary persistence of fetal hemoglobin from other conditions with increased percentage of fetal hemoglobin (Hb F)

Determining the distribution of Hb F within red blood cells

**Method Name**

Only orderable as a reflex. For more information see:

- HAEV1 / Hemolytic Anemia Evaluation, Blood
- HBEL1 / Hemoglobin Electrophoresis Evaluation, Blood
- MEV1 / Methemoglobinemia Evaluation, Blood
- REVE2 / Erythrocytosis Evaluation, Blood
- THEV1 / Thalassemia and Hemoglobinopathy Evaluation, Blood

Flow Cytometry

**NY State Available**

Yes

**Specimen****Specimen Type**

Whole Blood EDTA

**Ordering Guidance**

This test is for hereditary persistence of fetal hemoglobin only. For testing for possible fetal-maternal bleed, see FMB / Fetomaternal Bleed, Flow Cytometry, Blood.

**Specimen Required**

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- HAEV1 / Hemolytic Anemia Evaluation, Blood
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- MEV1 / Methemoglobinemia Evaluation, Blood
- REVE2 / Erythrocytosis Evaluation, Blood
- THEV1 / Thalassemia and Hemoglobinopathy Evaluation, Blood

**Specimen Minimum Volume**

0.5 mL

**Reject Due To**

Gross hemolysis	Reject
Gross lipemia	OK
Clotted blood	Reject

Specimen Stability Information

Specimen Type	Temperature	Time	Special Container
Whole Blood EDTA	Refrigerated	14 days	

Clinical & Interpretive

Clinical Information

More than 75% of the hemoglobin of the newborn is hemoglobin (Hb) F; it diminishes over a period of several months to adult levels, reducing to less than 2% by 1 year of age and less than 1% by 2 years of age.

Hb F may constitute 90% of the total Hb in patients with beta-thalassemia major or other combinations of beta thalassemia and fetal Hb (hereditary persistence of fetal hemoglobin [HPFH]) variants.

Hb F is often mildly to moderately elevated in sickle cell disease, aplastic anemia, acute leukemia, and myeloproliferative disorders such as juvenile myelomonocytic leukemia, hereditary spherocytosis, and alpha-thalassemia minor. It is commonly increased in hemoglobinopathies associated with hemolysis. Hb F increases to as high as 10% during normal pregnancy. Hb F is also increased due to medications such as hydroxyurea, decitabine, and lenalidomide. Elevation in Hb F has been cited as a discriminator between Diamond-Blackfan congenital pure red cell aplasia (elevated) and transient erythroblastopenia of childhood (normal), but whether this simply reflects the chronicity of anemia inherent to the former condition rather than a specific finding is unclear.

In the common (large deletional) form of the genetic trait HPFH, all of the erythrocytes contain Hb F. When tested by flow cytometry using specificity for Hb F, these HPFH cases display a homocellular distribution pattern of Hb F within the red blood cell population. Other causes of increased Hb F, including delta beta thalassemia, hydroxyurea, and some nondeletional HPFH variants, typically display a heterocellular distribution of Hb F within the erythrocytes, reflecting disparate populations of F cells and cells lacking Hb F. Quantification of Hb F percentage should be determined prior to flow cytometry of Hb F red blood cell distribution to establish the appropriateness of this test. The flow cytometry analysis of elevated Hb F levels is useful when Hb F percentage is 15% to 35% and the clinical differential diagnosis includes large deletional HPFH. Hb F percentages below 15% are likely not due to large deletional HPFH, and the causes of Hb F percentages above 35% are better confirmed by molecular and family studies.

Reference Values

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- HAEV1 / Hemolytic Anemia Evaluation, Blood
- HBEL1 / Hemoglobin Electrophoresis Evaluation, Blood
- MEV1 / Methemoglobinemia Evaluation, Blood
- REVE2 / Erythrocytosis Evaluation, Blood

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-THEV1 / Thalassemia and Hemoglobinopathy Evaluation, Blood

Reported as: Heterocellular, Homocellular, or Equivocal

**Interpretation**

Homocellular distribution of fetal hemoglobin (Hb) is found in large deletional hereditary persistence of fetal Hb.

Heterocellular distribution is found in delta beta thalassemia, medication induced, and other causes of increased Hb F.

An equivocal result indicates the pattern is not typical for either a homocellular or heterocellular distribution.

**Cautions**

When hemoglobin (Hb) F values are above 35%, most specimens show a homocellular pattern; this does not necessarily indicate hereditary persistence of fetal Hb. Clinical correlation is needed.

**Clinical Reference**

1. Kleihauer E, Braun H, Betke K. Demonstration von fetalem Hamoglobin in den Erythrocyten eines Blutaustriuchs. Klin Wschr. 1957;35(12):637-638
2. Shepard MK, Weatherall DJ, Conley CC. Semi-quantitative estimation of the distribution of fetal hemoglobin in red cell populations. Bull Johns Hopkins Hospital. 1962;110:293-310
3. Davis BH, Olsen S, Bigelow NC, Chen JC. Detection of fetal red cells in fetomaternal hemorrhage using a fetal hemoglobin monoclonal antibody by flow cytometry. Transfusion. 1998;38(8):749-756
4. Hoyer JD, Penz CS, Fairbanks VF, et al. Flow cytometric measurement of hemoglobin F in RBCs: diagnostic usefulness in the distinction of hereditary persistence of fetal hemoglobin (HPFH) and hemoglobin S-hPFH from other conditions with elevated levels of hemoglobin F. Am J Clin Pathol. 2002;117(6):857-863
5. Stephens AD, Angastiniotis M, Baysal E, et al. International Council for The Standardisation of Haematology (ICSH). ICSH recommendations for the measurement of haemoglobin F. Int J Lab Hematol. 2012;34(1):14-20

**Performance****Method Description**

This assay uses a flow cytometric method with a monoclonal antibody to hemoglobin (Hb) F. Specimens are analyzed by single-color flow cytometry using fluorescein anti-Hb F. In normal adults, a single peak is seen with minimal fluorescence, which corresponds to Hb A. In neonates, a single peak with bright fluorescence is seen, which corresponds to Hb F. In cases of hereditary persistence of fetal Hb (HPFH) only, a single peak is observed, which has a fluorescence intensity intermediate between the normal Hb A and Hb F peaks. This pattern corresponds to the homocellular (pancellular) pattern obtained by the Kleihauer-Betke (K-B) method. In contrast, specimens from infants, transfused neonates, and cases of beta-thalassemia or delta/beta-thalassemia show both Hb A and Hb F peaks, corresponding to the heterocellular pattern of the K-B method. In patients with Hb S/HPFH, a single peak was observed in contrast to patients with homozygous S in which 2 peaks were observed. (Package insert: Invitrogen Fetal Hemoglobin Test Kit with FITC-conjugated Monoclonal Antibody Directed to HbF. Life Technologies Corporation; MAN 0003641, Rev 3.02, 11/21/2019)

**PDF Report**

No

Day(s) Performed

Monday through Friday

Report Available

3 to 5 days

Specimen Retention Time

1 week

Performing Laboratory Location

Mayo Clinic Laboratories - Rochester Main Campus

Fees & Codes

Fees

- Authorized users can sign in to [Test Prices](#) for detailed fee information.
- Clients without access to Test Prices can contact [Customer Service](#) 24 hours a day, seven days a week.
- Prospective clients should contact their account representative. For assistance, contact [Customer Service](#).

Test Classification

This test has been modified from the manufacturer's instructions. Its performance characteristics were determined by Mayo Clinic in a manner consistent with CLIA requirements. This test has not been cleared or approved by the US Food and Drug Administration.

CPT Code Information

88184

LOINC® Information

Test ID	Test Order Name	Order LOINC® Value
HPFH	Hb F Distribution, B	4579-9

Result ID	Test Result Name	Result LOINC® Value
8270	Hb F Distribution, B	4579-9
2104	Interpretation	59466-3